

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/005006

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C12N15/11 A61K31/7088

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HYER M.L. ET AL.: "Downregulation of c-FLIP sensitizes DU145 prostate cancer cells to Fas-mediated apoptosis" CANCER BIOLOGY & THERAPY, vol. 1, no. 4, July 2002 (2002-07), pages 401-406, XP008052890 the whole document	5-11,14, 18-24, 27, 31-37,40
Y	USLU R. ET AL.: "Chemosensitization of human prostate carcinoma cell lines to anti-Fas-mediated cytotoxicity and apoptosis" CLINICAL CANCER RESEARCH, THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, US, vol. 3, no. 6, June 1997 (1997-06), pages 963-972, XP002093792 ISSN: 1078-0432 the whole document	5-11,14, 18-24, 27, 31-37,40
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the International search

27 September 2005

Date of mailing of the International search report

11/10/2005

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

Internat'l Application No  
PCT/GB2004/005006

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	THÉARD D. ET AL.: "Etoposide and Adriamycin but not Genistein can activate the checkpoint kinase Chk2 independently of ATM/ATR" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 289, 2001, pages 1199-1204, XP002346591 abstract	3
A	GUROVA K.V. ET AL.: "Cooperation of two mutant p53 alleles contributes to Fas resistance of prostate carcinoma cells" CANCER RESEARCH, vol. 63, 1 June 2003 (2003-06-01), pages 2905-2912, XP002346592 page 2911, left-hand column	13, 26, 39
X	IWASE M. ET AL.: "Enhanced susceptibility of oral squamous cell carcinoma cell lines to Fas-mediated apoptosis by Cisplatin and 5-Fluorouracil" INTERNATIONAL JOURNAL OF CANCER, vol. 106, 10 September 2003 (2003-09-10), pages 619-625, XP008052887	5-11, 13, 14, 18-24, 26, 27, 31-37, 39, 40
Y	the whole document	15, 28, 41, 43, 44
A	WAKASA T. ET AL.: "The combination of ionizing radiation and expression of a wild type p53 gene via recombinant adenovirus induced a prominent tumour suppressing effect in human oral squamous cell carcinoma" THE BRITISH JOURNAL OF RADIOLOGY, vol. 75, 2002, pages 657-662, XP002346593 page 660 - page 661	13, 26, 39
Y	WO 03/035868 A (RIBOPHARMA AG (DE); WAJANT; PFIZENMAIER; LIMMER; KREUTZER; VORNLOCHER) 1 May 2003 (2003-05-01) page 9	15, 28, 41, 43, 44
A	SIEGMUND D. ET AL.: "Selective inhibition of FLICE-like Inhibitory Protein (FLIP) expression with small interfering RNA oligonucleotides (siRNAs) is sufficient to sensitize tumor cells for TRAIL-induced apoptosis" MOLECULAR MEDICINE, BLACKWELL SCIENCE, CAMBRIDGE, MA, US, vol. 8, no. 11, November 2002 (2002-11), pages 725-732, XP009005569 ISSN: 1076-1551 the whole document	----- -/-

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Inte      nal Application No  
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE EMBL-EBI      1 July 1999 (1999-07-01), "Homo sapiens      FLICE-like inhibitory protein long form      mRNA, complete cds."      XP002346640      Database accession no. U97074      the whole document</p> <p>-----</p>	
Y	<p>KAMARAJAN P. ET AL.: "Up-regulation of      FLIP in cisplatin-selected HeLa cells      causes cross-resistance to CD95/Fas death      signalling"      BIOCHEMICAL JOURNAL,      vol. 376, no. 1,      15 November 2003 (2003-11-15), pages      253-260, XP002346594      the whole document</p> <p>-----</p>	3,4,17, 30
Y	<p>MAY E. ET AL.: "Endogenous HeLa p53      proteins are easily detected in HeLa cells      transfected with mouse deletion mutant p53      gene"      ONCOGENE,      vol. 6, no. 8, 1991, pages 1363-1366,      XP008053053      the whole document</p> <p>-----</p>	3,4,17, 30
A	<p>PEDERSEN I.M. ET AL.: "The triterpenoid      CDDO induces apoptosis in refractory CLL B      cells"      BLOOD,      vol. 100, no. 8,      15 October 2002 (2002-10-15), pages      2965-2972, XP002346596      the whole document</p> <p>-----</p>	1
A	<p>POULAKI V. ET AL.: "Fas-mediated      apoptosis in neuroblastoma requires      mitochondrial activation and is inhibited      by FLICE inhibitor protein and bcl-2"      CANCER RESEARCH,      vol. 61, 15 June 2001 (2001-06-15), pages      4864-4872, XP002346597      the whole document</p> <p>-----</p>	1
A	<p>MICHEAU O.: "Cellular FLICE-inhibitory      protein: an attractive therapeutic target      ?"      EXPERT OPINION ON THERAPEUTIC TARGETS,      ASHLEY PUBLICATIONS, LONDON, GB,      vol. 7, no. 4, August 2003 (2003-08),      pages 559-573, XP009045505      ISSN: 1472-8222      page 564 - page 566</p> <p>-----</p>	

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 1-15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/GB2004/005006

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03035868	A 01-05-2003	NONE	